中 山 醫 學 大 學 附 設 醫 院

膀 胱 癌 診 療 指 引

臨床指引參考台灣國家衛生研究院、與美國 NCCN 版本
再依據中山醫學大學附設醫院泌尿道癌小組經驗作編修
泌尿道癌醫療小組

2017/12/01 Version 9.0
2016/11/04 Version 8.0
2015/11/20 Version 7.0
2014/12/19 Version 6.0
2013/12/27 Version 5.0
2012/12/07 Version 4.0
2011/11/18 Version 3.1
2011/01/21 Version 3.0
2010/05/28 Version 2.0
2009/12/16 Version 1.0

癌症委員會主任委員	癌症委員會執行長	癌症防治中心主任	團隊負責人

修訂內容

<table>
<tr><th>頁數</th><th>原文</th><th>修訂/新增</th></tr>
<tr><td>第 1 頁</td><td>前言：
2012 年膀胱癌死亡人數占全部惡性腫瘤死亡人數的 3.5%；死亡率排行於男性為第 11 位、女性為第 12 位
Practice Guide-lines in Bladder Cancer V1 2016 版</td><td>前言：修訂為-
2014 年膀胱癌死亡人數占全部惡性腫瘤死亡人數的 2.07%；死亡率排行於男性為第 12 位、女性為第 15 位
Practice Guide-lines in Bladder Cancer V9 2017 版</td></tr>
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<tr><th>TNM</th><th>Described</th><th>stage</th></tr>
<tr><td>Ta</td><td>Noninvasive papillary carcinoma</td><td>0a</td></tr>
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<tr><td>T1</td><td>Tumor invades subepithelial connective tissue</td><td>I</td></tr>
<tr><td>T2</td><td>Tumor invades superficial muscle propria</td><td rowspan="3">II</td></tr>
<tr><td>T2a</td><td>Tumor invades superficial muscle propria(inner half)</td></tr>
<tr><td>T2b</td><td>Tumor invades deep muscle propria (out half)</td></tr>
<tr><td>T3a</td><td>Microscopically</td><td rowspan="2">III</td></tr>
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IV</td></tr>
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<tr><td>N1</td><td>Metastasis in a single regional lymph node in the true pelvis
（hypogastric, obturator, external iliac, or presacral lymph node）</td><td rowspan="5">IV</td></tr>
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<tr><td>M0</td><td>No distant metastasis</td></tr>
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Chung Shan Medical University Hospital 膀胱癌治療指引 Clinical Guideline 2018 version9.0

NX	Lymph nodes cannot be assessed
N0	No lymph node metastasis
N1	Single regional lymph node metastasis in the true pelvis (perivesical, obturator, internal and external iliac, or sacral lymph node)
N2	Multiple regional lymph node metastasis in the true pelvis (perivesical, obturator, internal and external iliac, or sacral lymph node metastasis)
N3	Lymph node metastasis to the common iliac lymph nodes

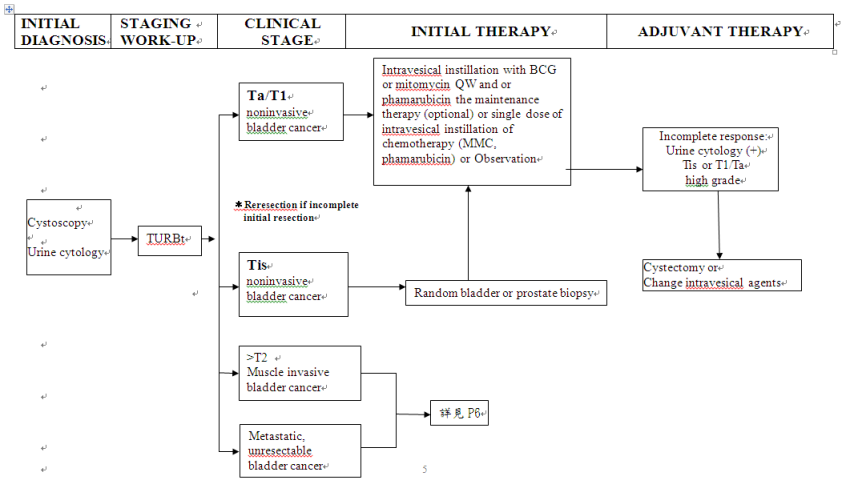
M0	No distant metastasis
M1	Distant metastasis
M1a	Distant metastasis limited to lymph nodes beyond the common iliacs
M1b	Non-lymph node distant metastasis

When T is…	And N is…	And M is…	Then the stage group is…
Ta	N0	M0	0a
Tis	N0	M0	0is
T1	N0	M0	I
T2a	N0	M0	II
T2b	N0	M0	II
T3a, T3b, T4a	N0	M0	IIIA
T1 - T4a	N1	M0	IIIA
T1 - T4a	N2, N3	M0	IIIB
T4b	Any N	M0	IVA
Any T	Any N	M1a	IVA
Any T	Any N	M1b	IVB

第 6 頁

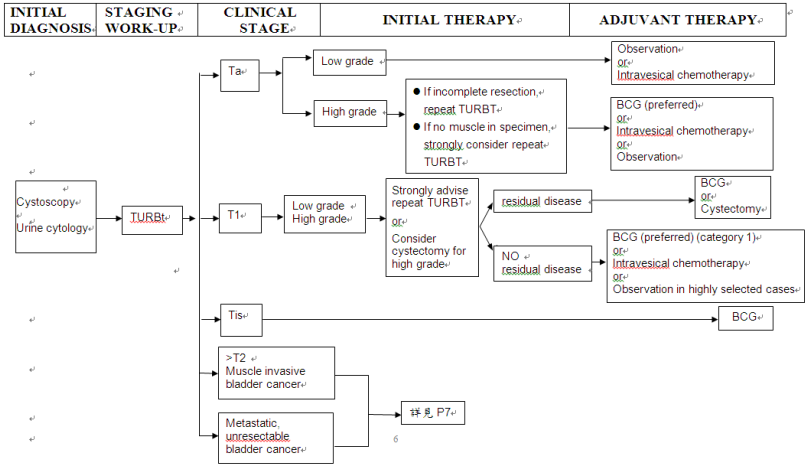
治療指引：

五、膀胱癌治療指引



治療指引：修訂為-

五、膀胱癌治療指引



第 7 頁

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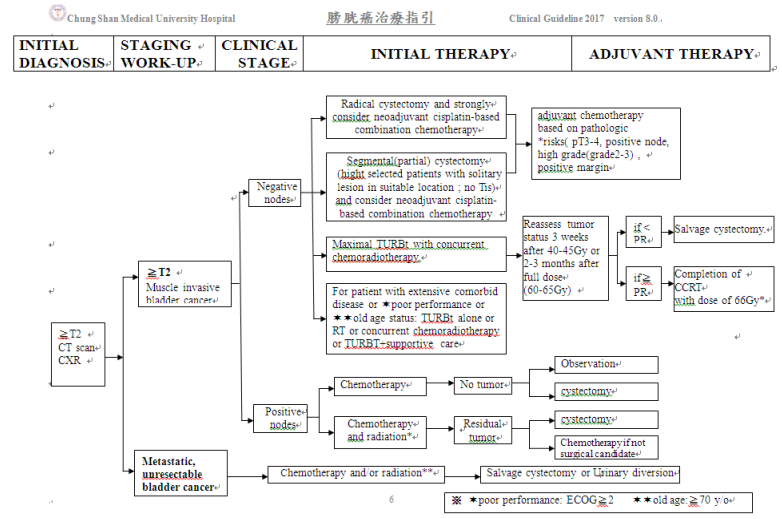

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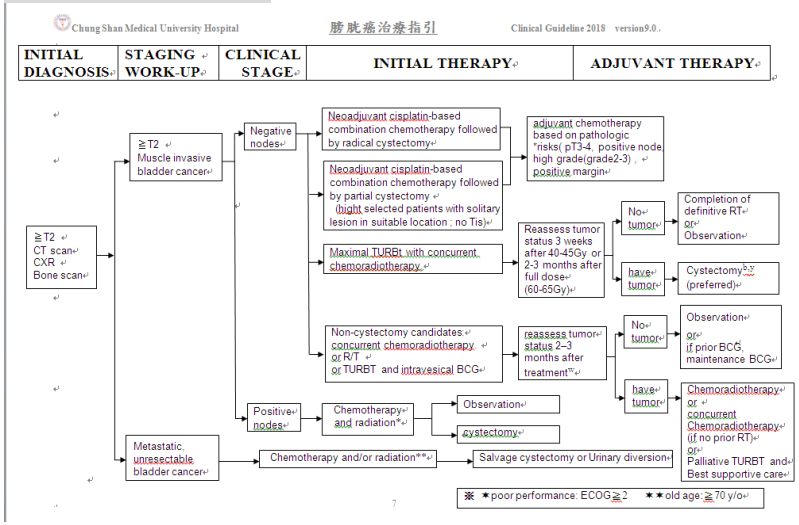

目 錄

一、前言

本共識手冊內所提之各種診治意見，為原則性之建議，希望能為癌症患者及其家屬提供一個正確的指引；但對臨床醫師之醫療行為無絕對之法律性約束力！由於醫藥科技持續在進步，每位患者的病情亦不盡相同；醫師應就病人之病情做個別的考量，病人和家屬亦應與醫師溝通討論，以決定最適當之診治方式。

在台灣地區，膀胱惡性腫瘤病患每年均有增加的趨勢，男性發生率約為女性的2.5倍。2014年膀胱癌死亡人數占全部惡性腫瘤死亡人數的2.07%；死亡率排行於男性為第12位、女性為第15位。有鑒於此，本院自2009年6月開始由泌尿外科、病理科、醫學影像部、放射腫瘤科與血液/腫瘤內科組成膀胱癌團隊。本院膀胱癌治療，藉由科際合作及定期開會討論，得到很好的治療成果。尤其是本院的病人群中有一定的比例是腎移植後併發癌病的泌尿移形上皮細胞癌，他們的移形上皮細胞癌，常是多發性，散見於病人本身已衰竭的腎臟，或是輸尿管及膀胱上，我們認為若能在病人發生血尿或腰痛時作篩檢，將可提早發現癌症這個併發症。這也讓我們累積了相當豐富的處理經驗及成為中台灣腎移植病人照顧中心。

本膀胱癌診斷及治療指引的建立，除了依據已發表的實證醫學證據及專家意見外，並參考國家衛生研究院膀胱癌臨床指引、美國National Comprehensive Cancer Network (NCCN) 的 Practice Guide-lines in Bladder Cancer V1 2018版、及中山醫學大學附設醫院膀胱癌治療經驗進行編修。

二、症狀、診斷和檢查

膀胱癌的一些常見症狀包括：

(1)血尿（顏色呈淺褐色至深紅色）。

(2)解尿疼痛。

(3)頻尿或是常有尿意感但卻無小便。

當上述這些症狀產生時，並不確定是膀胱癌。也有可能是因為感染，良性腫瘤、膀胱結石或其它原因所造成，必須靠醫師來確定診斷。（所以當有上述症狀時，應去看家庭醫師或泌尿科醫師，泌尿科醫師是專長於泌尿系統疾病的醫師）。任何疾病都應立刻去看醫師，如此才能早期診斷，早期治療。

為了找出症狀的原因，醫生會詢問患者的病史並執行一些身體檢查。身體檢查包括直腸或陰道檢查，來幫助醫師檢查是否有腫瘤的存在。另外，尿液檢體會被送到實驗室檢驗來檢查是否有血液和癌細胞的存在。

會使用膀胱鏡檢查直接檢查膀胱，檢查過程可能需要採局部或全身麻醉，可藉由膀胱鏡取出組織標本做切片檢查，這是唯一可以確定是否有癌細胞的方法。如果整個癌症在膀胱鏡下切片時被移除，膀胱癌便在單一的治療程序下被診斷及治療。

膀胱癌的分期可能在診斷的同時就可以確定，或者它可能需要再做一些其它的檢查。這些檢查可能包括影像學檢查--電腦斷層掃描、磁振造影、超音波、靜脈腎盂攝影術、骨骼掃描或胸腔 X 光。

三、組織病理分類與分化

■膀胱泌尿上皮癌的病理組織分化依2004 WHO grading分為：

Urothelial papilloma
Papillary urothelial neoplasm of low malignant potential (PUNLMP)
Low-grade papillary urothelial carcinoma
High-grade papillary urothelial carcinoma

四、分期

依據AJCC/UICC TNM, 8th edition (2018)：

TNM	Described
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Ta	Non-invasive papillary carcinoma
Tis	Urothelial carcinoma in situ:“flat tumor”
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M0	**No distant metastasis**
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M1a	**Distant metastasis limited to lymph nodes beyond the common iliacs**
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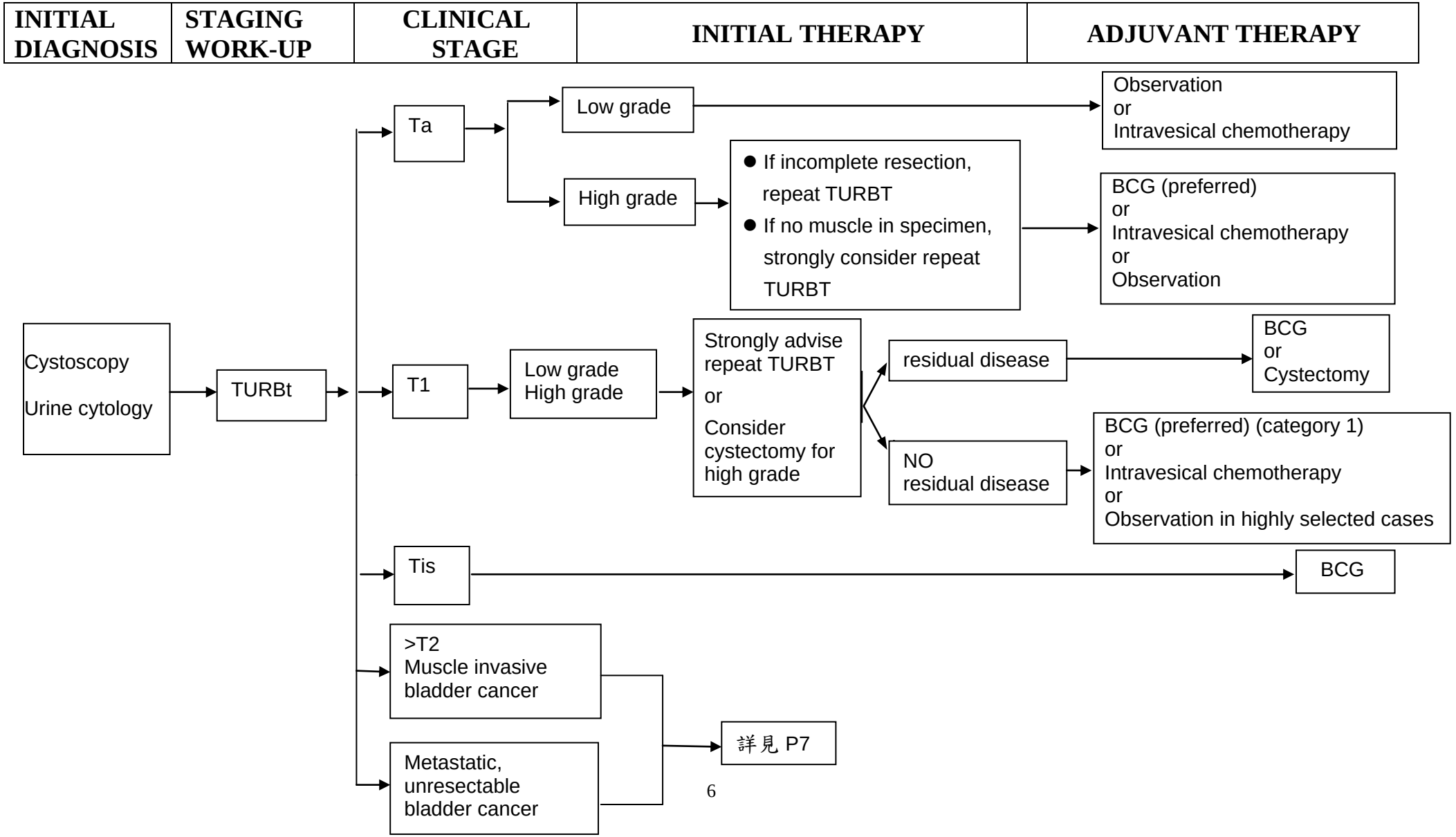
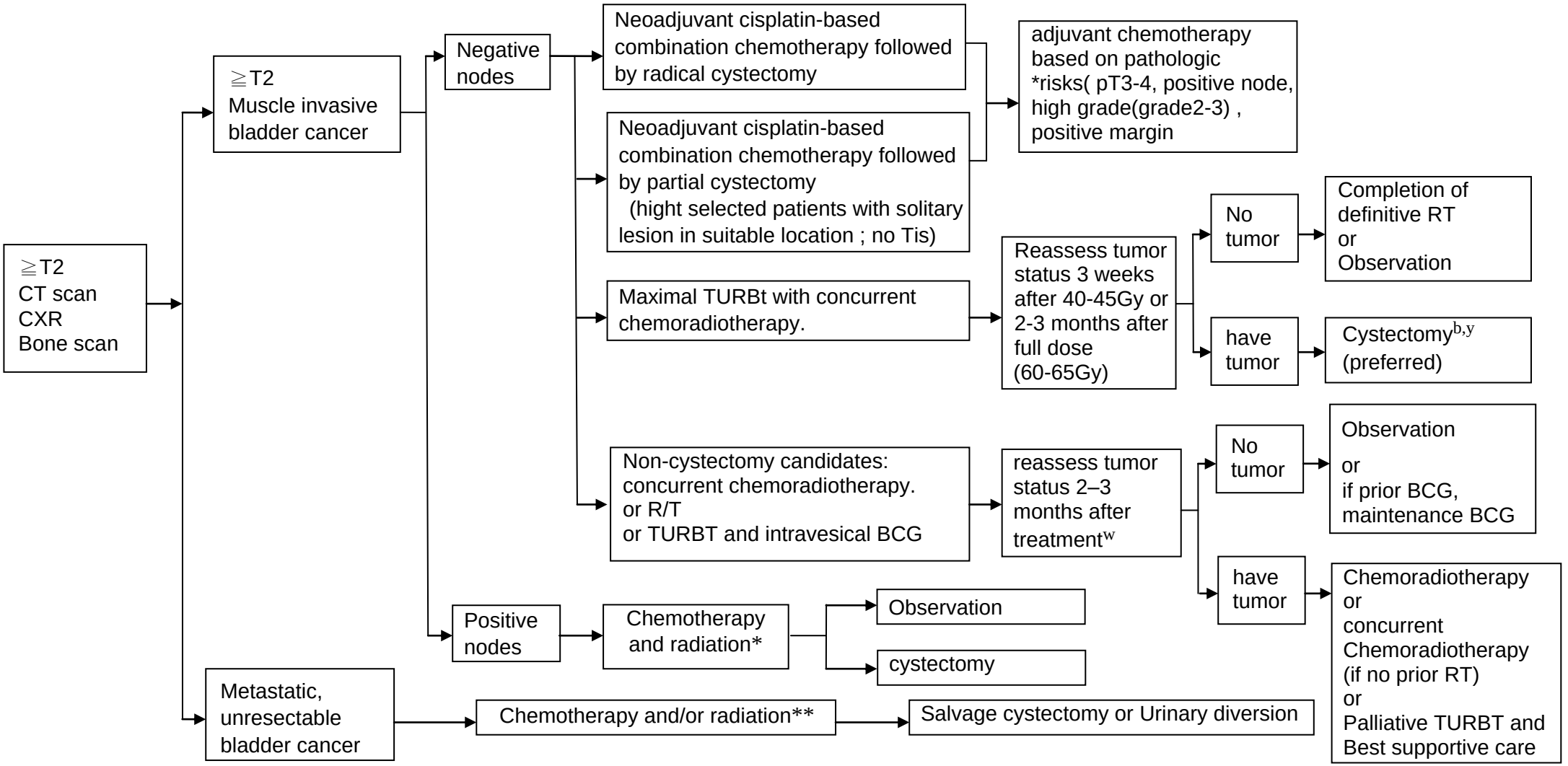
When T is…	And N is…	And M is…	Then the stage group is…
Ta	**N0**	**M0**	**0a**
Tis	**N0**	**M0**	**0is**
T1	**N0**	**M0**	**I**
T2a	**N0**	**M0**	**II**
T2b	**N0**	**M0**	**II**
T3a, T3b, T4a	**N0**	**M0**	**IIIA**
T1 - T4a	**N1**	**M0**	**IIIA**
T1 - T4a	**N2, N3**	**M0**	**IIIB**
T4b	**Any N**	**M0**	**IVA**
Any T	**Any N**	**M1a**	**IVA**
Any T	**Any N**	**M1b**	**IVB**

五、膀胱癌治療指引

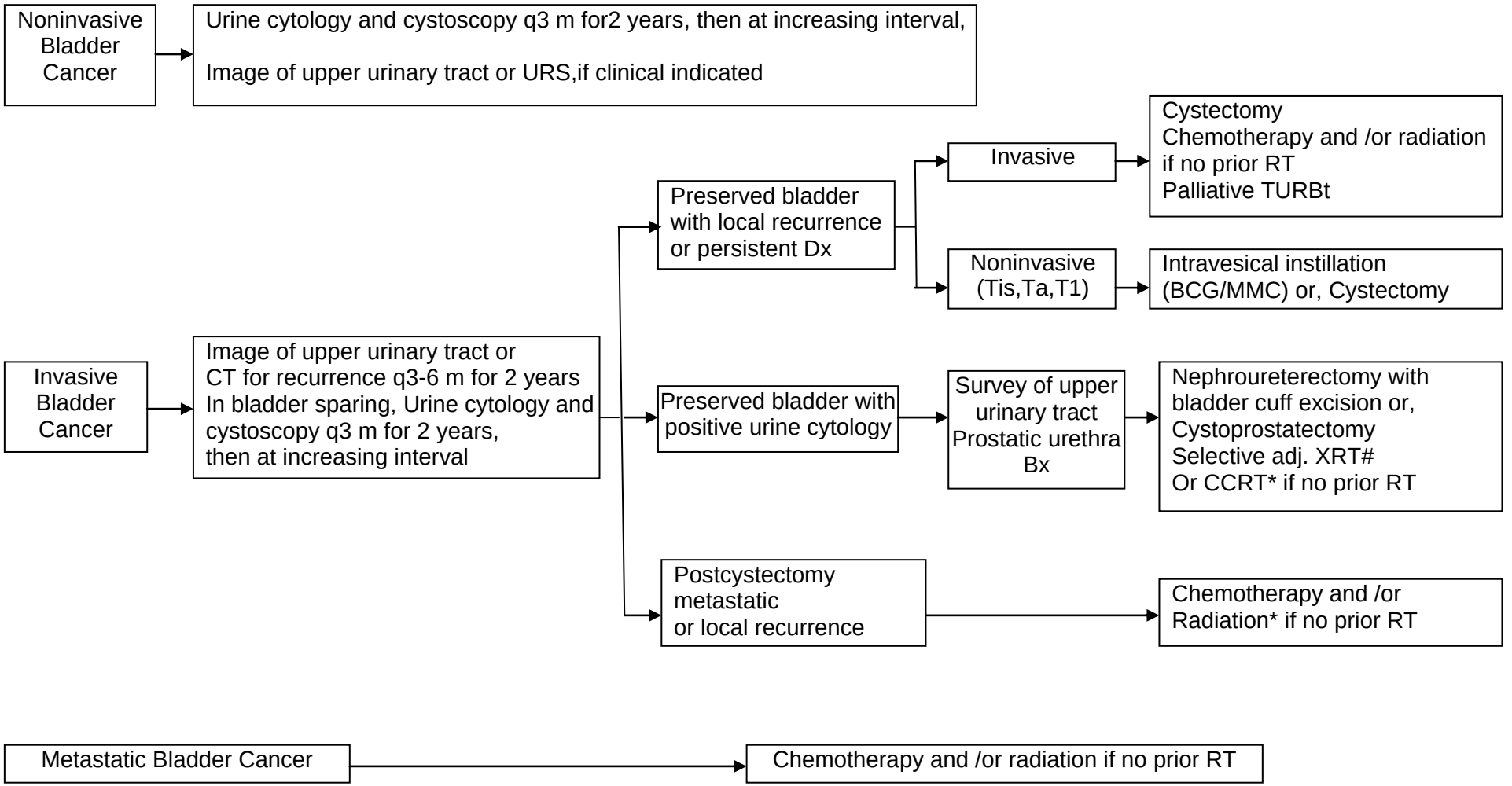

INITIAL DIAGNOSIS
STAGING WORK-UP
CLINICAL STAGE
INITIAL THERAPY
ADJUVANT THERAPY
Cystoscopy
Urine cytology
TURBt
Ta
Low grade
Observation or Intravesical chemotherapy
High grade
If incomplete resection, repeat TURBT
If no muscle in specimen, strongly consider repeat TURBT
BCG (preferred) or Intravesical chemotherapy or Observation
T1
Low grade
High grade
Strongly advise repeat TURBT or Consider cystectomy for high grade
residual disease
BCG or Cystectomy
NO residual disease
BCG (preferred) (category 1) or Intravesical chemotherapy or Observation in highly selected cases
Tis
BCG
>T2 Muscle invasive bladder cancer
Metastatic, unresectable bladder cancer
詳見 P7

INITIAL DIAGNOSIS	STAGING WORK-UP	CLINICAL STAGE	INITIAL THERAPY	ADJUVANT THERAPY



※ ✶poor performance: ECOG≧2 ✶✶old age:≧70 y/o

FOLLOW – UP	TREATMENT OF RECURRENCE OR PERSISTENT DISEASE



六、膀胱癌的外科治療處置

Principles of Surgical Management

TURBt: (Ta/T1)

- Adequate resection with muscle if papillary high-grade lesion
- Reresection if incomplete initial resection, no muscle in specimen or large lesion

TURBt: Tis

- Multiple random biopsies
- Biopsy adjacent to tumor
- Prostate urethral biopsies

TURBt: invasive

Repeat resection:

- Any T1, any grade
- If no muscle in biopsy
- Small fragment of T2 insufficient to attribute risk
- Repeat TURBt should be considered if first TURBt does not allow adequate staging or attribution of risk factor for treatment selection or when using bladder preserving treatment by chemotherapy and/or RT

SEGMENTAL (PARTIAL) CYSTECTOMY

- Solitary lesion in location amenable to partial resection with adequate margin, no Tis
- Pelvic lymphadenectomy may be performed in conjunction with the partial cystectomy

RADICAL CYSTECTOMY

- Radical cystectomy should include bilateral node dissection at a minimum including common，internal and external iliac nodes and obturator nodes

七、膀胱癌的化學及放射線治療

Principles of chemotherapy

Intravesical chemotherapy for Tis ,Ta 及 T1 cancer

Mitomycin (Miomycin-C) 30mg qw x6 and /or qm x3
Phamarubicin 30mg qw x6 and/or qm x3
BCG 81 mg qw (x6) since 2nd post-op week and/or qw (x3) since 3rd post-op month, qw (x3) since 6th post-op month, qw (x3) since 12th post-op month Intravesical chemotherapy

Neoadjuvant or adjuvant chemotherapy for stage II, III and non-metastatic stage IV cancer

MVAC

Methotrexate	30 mg/m^2 iv			d1, 15 and 22
Vinblastine	3 mg/m^2 iv			d2, 15 and 22
Doxorubicin	30 mg/m^2 iv			d2
Cisplatin	70 mg/m2 iv	or	Carboplatin AUC 4-6	d1 or 2
Q4w x 3 cycles				

Grossman HB et al. Neuadjuvant chemotherapy plus cystectomy compared with cystectomy alone for locally advanced bladder cancer. N Eng J Med 2003; 349:859

Gemcitabine (自費)+ Cisplatin (Carboplatin)

Gemcitabine	800 - 1000 mg/m^2 iv			d1, 8 and 15
Cisplatin	70 mg/m2 iv	or	Carboplatin AUC 4-6	d1
Q4w x 3 cycles				

Von der Maase H et al. Gemcitabine and cisplatin versus methotrexate, vinblastine, doxorubicin and cisplatin in advanced or metastatic bladder cancer: results of a large, randomized, multinational, multicenter, phase III study. J Clin Oncol 2000; 18:3068

CMV

Cisplatin	70 mg/m^2 iv	d2
Vinblastine	4 mg/m^2 iv	d1, 8
Methotrexate	30 mg/m^2 iv	d1, 8
Q3w x 3 cycles		

Internationa Collaboration of Trialists. Neoadjuvant cisplatin, methotrexate, and vinblastine chemotherapy for muscle invasive bladder cancer: a randomized controlled trial. Lancet 1999; 354:533

Concurrent chemoradiation for stage II, III and non-metastatic stage IV cancer

Cisplatin

Cisplatin	30-40 mg/m2 iv	or	Carboplatin AUC 2	d1
Q1w x 6 cycles				

Tunio MA et al. Bladder preservation by neoadjuvant chemotherapy followed by concurrent chemoradiation for muscle-invasive bladder cancer: experience at Sindh Institute of Urology & Transplantation (SIUT). J Pak Med Assoc 2011; 61:6.

Chemotherapy for metastatic cancer

Principles of systemic therapy

First-line chemotherapy for locally advanced or metastatic disease

	Standard regimens	Alternate regimens for select patients
Cisplatin eligible	• Gemcitabine and cisplatin4 (category 1) • DDMVAC with growth factor support (category 1)	
Cisplatin ineligible with poor kidney function or poor PS	• Gemcitabine and carboplatin	• Gemcitabine • Gemcitabine and paclitaxel
Cisplatin ineligible due to hearing/ neuropathy but with good kidney function, and good PS		• Ifosfamide, doxorubicin and gemcitabine

Second-line systemic therapy for locally advanced or metastatic disease

Standard regimens	Alternate regimens for select patients
• Atezolizumab • Paclitaxel or docetaxel (自費) • Gemcitabine • Pemetrexed (自費)	• Nab-paclitaxel (自費) • Ifosfamide • Methotrexate • Ifosfamide, doxorubicin, and gemcitabine • Gemcitabine and paclitaxel (自費) • Gemcitabine and cisplatin • DDMVAC

MVAC

Methotrexate	30 mg/m^2 iv			d1, 15 and 22
Vinblastine	3 mg/m^2 iv			d2, 15 and 22
Doxorubicin	30 mg/m^2 iv			d2
Cisplatin	70 mg/m2 iv	or	Carboplatin AUC 4-6	d1 or 2
Q4w x 6 cycles				

Han KS et al. Methotrexate, vinblastine, doxorubicin and cisplatin combination regimen as salvage chemotherapy for patients with advanced or metastatic transitional cell carcinoma after failure of gemcitabine and cisplatin chemotherapy. Br J Cancer 2008; 98:86.
Logothetis CJ et al. A prospective randomized trial comparing MVAC with CISCA chemotherapy for patients with metastatic urothelial tumors. J Clin Oncol 1990; 8:1050.

Gemcitabine + Cisplatin(Carboplatin)

Gemcitabine	800 - 1000 mg/m^2 iv	d1, 8 and 15
Cisplatin	70 mg/m^2 iv	d2
Q4w x 6 cycles		

von der Maase H et al. Gemcitabine and cisplatin versus methotrexate, vinblastine, doxorubicin and cisplatin in advanced or metastatic bladder cancer: results of a large, randomized, multinational, multicenter, phase III study. J Clin Oncol 2000; 18:3068

Paclitaxel +/- Cisplatin(Carboplatin)

Paclitaxel	80 mg/m^2 iv			d1, 8, 15
Cisplatin	70 mg/m2 iv	or	Carboplatin AUC 4-6	d1
Q4w x 6 cycles				

von der Maase H et al. Gemcitabine and cisplatin versus methotrexate, vinblastine, doxorubicin and cisplatin in advanced or metastatic bladder cancer: results of a large, randomized, multinational, multicenter, phase III study. J Clin Oncol 2000; 18:3068

Principles of radiation

Selective adjuvant radiotherapy #

If margin positive/residual or LN positive，**dose of 50~70Gy** depends on the tumor position and the patient condition

Definitive radiotherapy *

60~70Gy，depended on the tumor position and the patient status.

Palliative radiotherapy **

20~40Gy，depended on the disease condition and the patient status.

八、安寧緩和照護原則

若預期疾病難以治癒時，病人存活期小於 6 個月便適合安寧療護(Pomeranz & Brustman, 2005；Waldrop & Rinfrette, 2009) 。若藉由症狀、檢驗數據、及確切的腫瘤診斷，證實臨床上該惡性腫瘤已經廣泛侵犯、或進展快速；功能分數（Palliative Performance Scale）低於 70%；拒絕進一步腫瘤治癒性治療，或者在治療之下仍持續惡化者，即可轉介緩和醫療團隊（彭等，2006）。

九、參考文獻

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十、膀胱癌Stage IV完治率定義

1. STAGE IV 接受化療一次。
2. STAGE IV 接受放射治療一個療程。
3. STAGE IV 接受安寧緩和。